

*Wormley (Theo. G.)*  
MEDICAL CHEMISTRY AND TOXICOLOGY.

AN ADDRESS

DELIVERED BEFORE THE

INTERNATIONAL MEDICAL CONGRESS,

AT

PHILADELPHIA,

September 5, 1876.



BY

THEO. G. WORMLEY, M.D., Ph.D., LL.D.,

PROFESSOR OF CHEMISTRY AND TOXICOLOGY IN STARLING MEDICAL COLLEGE, COLUMBUS, OHIO.

[Extracted from the Transactions.]

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## A D D R E S S .

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WHEN it is remembered that nearly all human thought and labor are devoted to the promotion of the welfare of the human body, and that agriculture, manufactures, and commerce have this as their chief end, it will not be deemed strange that a science so comprehensive and withal so flexible in its applications as Chemistry, should be laid under contribution to preserve that body in health, or to restore that health when impaired. Before chemistry had become a true science, its aid was invoked by the old alchemists in their search for the "Elixir of Life." A universal remedy was the dream of many a toiler in secret places, whose occult science had for him a strange fascination. There were among the Arabians many who, in their rude way, applied such chemical knowledge as they possessed to the discovery of new medicines. The same was true of the earlier physicians of Europe. There was everywhere an effort to make nature reveal some secret which might be turned to account in the healing art. This, more than any other, was deemed the true function of Chemistry.

It was not until Bacon announced the true method of scientific investigation, and declared that the Kingdom of Science, like the Kingdom of Heaven, was to be entered as a child, rather than with the spirit of a dictator, that the mists of earlier times were gradually swept away, and the path prepared for the appearance of Science with exact methods and with exact results.

It is now only about a century since Chemistry took shape as a Science. The labors of Black, Priestley, Scheele, Lavoisier, and others showed that a vast field of research lay before them. For a century chemists have been exploring this field, and have taken possession of many a spot, and secured permanent title-deeds for posterity; but, it must be confessed, that a century is far too short for the survey of the whole domain, and our descendants will have ample scope and incentive for the profoundest labor and research. Only two years since, the chemists of Great Britain and America celebrated the centennial of Chemistry, dating the birth of the science from the discovery of Oxygen by the distinguished Priestley, August 1, 1774. The commemoration in this country took place at Northumberland, Pa., the American home of Dr. Priestley. The general progress of the century was there ably set forth by men of note in their several departments of investigation. The very valuable address of Prof. Benjamin Silliman, on this occasion, on *American Contributions to Chemistry* (a complete compendium to which we are greatly indebted) shows that in this country we have not been idle in advancing this department of science.

After the discovery of oxygen, nitrous oxide, and other gases, by



Priestley and others, Sir Humphry Davy, then a young man with majority unreached, was employed at Bristol, through the generosity of Messrs. Watt and Wedgwood, to undertake a careful series of experiments with gases as remedial agents. So important and intimate is the connection between chemistry and medicine, that we should naturally look to those who feel the imperative need of this science in its sanitary applications, for the best labors in the science. There could be no other incentive more potent. The air and vapors we breathe, the food we eat, the fluids we drink, the medicines we take, and the poisons we seek to avoid, all come within the range of the analyst, and his words of counsel and caution are to be heeded. In this field of labor many eminent chemists have labored with exclusive devotion, while others, as Davy, Scheele, and Liebig, commenced their distinguished careers as pharmacists, and may be said to have emerged from the apothecary's shop. Indeed, we may not overlook the close connection between chemistry and pharmacy. As we trace the history of medical chemistry in the United States, it will be seen that the contributions of the pharmacists have been so many and various, that the historian must give them a high and honorable place in the annals of American progress.

One hundred years ago we find that the only medical college in the land, with an occupied chair of chemistry, was the Philadelphia Medical College, soon after (1791) merged into the University of Pennsylvania, the institution in whose halls we are now assembled, an institution not only venerable in years, but renowned for the great and noble work it has accomplished. The occupant of this chair, elected August 1, 1769, was none other than Dr. Benjamin Rush, distinguished alike for his professional labors, which brought honor upon medical science, and for his devoted patriotism in the dark days when our national independence was won. He graduated at Princeton, and afterwards studied medicine in Philadelphia, Edinburgh, London, and Paris. While in Edinburgh he studied chemistry with the eminent Dr. Joseph Black. He was one of the signers of the Declaration of Independence, which this centennial year commemorates. In 1777 he was made surgeon-general of the army in the middle department. Ever a distinguished physician and medical professor, ever active in all public and philanthropic movements, his long life was one of singular usefulness and honor, and no name in our annals should be mentioned with more reverence and respect than that of Benjamin Rush, the earliest American professor of chemistry. The only other chair of chemistry in the colonial days was that established in William and Mary College, Virginia, in 1774, and filled by the Rev. James Madison.

In 1779 a professorship of chemistry and natural philosophy was established in the literary department of the University of Pennsylvania. Thus two of the first three chemical professorships in America were established in Philadelphia. In the medical department of Harvard University, Aaron Dexter was elected Professor of Chemistry and Materia Medica in 1783; and in 1792 Dr. Samuel Latham Mitchell was elected Professor of Chemistry in Columbia College, New York. Dr. Mitchell graduated in medicine in Edinburgh in 1786. Two years after entering upon his professorship of Chemistry, he published an essay on the *Nomenclature of the New Chemistry*. In 1797 he, with others, established the *Medical Repository*, the first scientific periodical ever published in the United States. He is now widely known as an early student of



natural history, and his publications on zoological subjects are yet prized.

In 1795 Professor John McLean, a young chemist of Scotland, was elected Professor of Chemistry in Nassau Hall, Princeton. In 1803 Professor Benjamin Silliman, the first professor of chemistry in Yale College, entered upon his duties. He became widely known as an able and eloquent expounder of chemical science. In 1818 he established *The American Journal of Science and Arts*, which became, more than any American journal, the means of disseminating discoveries in chemistry and in cognate sciences. His name will ever remain an honored one in the history of American science.

The work done in chemistry in the medical schools has not always been marked by scientific thoroughness; indeed, in too many cases, very little practical benefit has resulted from the lectures, often only heard to be forgotten. But a change is now being effected in this respect, and we note with satisfaction that a two years' course of systematic laboratory practice is made part of the regular curriculum of study in the Medical Department of Harvard University.

The earlier professors of chemistry in the Medical Schools did not contribute largely to the advancement of the science in the way of original research. The science was in its infancy, and the circumstances surrounding them were not generally such as to awaken that measure of enthusiasm which is necessary to scientific discoveries. A marked exception, however, is found in the case of Dr. Robert Hare, who became Professor of Chemistry in the University of Pennsylvania in 1818. In his youth he was a member of the Chemical Society of Philadelphia, to which belonged Priestley, Seybert, and others. At the early age of twenty, he announced the discovery of the oxy-hydrogen blowpipe, which at once gave him distinction in both hemispheres. This became a valuable instrument in certain departments of chemical investigations, and in the arts. Dr. Hare had great mechanical skill, and with his ingenious apparatus was enabled to perform experiments with great brilliancy and success. In addition to many valuable contributions, he published, in 1828, a *Compendium of Chemistry*, a valuable and useful work at the time. In this connection it should be mentioned that in 1819 Dr. John Gorham, Professor of Chemistry in the Medical Department of Harvard University, published the first original systematic treatise on chemistry ever issued in this country, entitled the *Elements of Chemical Science*, a work in two volumes, which reflected great credit upon its author. It should be stated, however, that there had been, before this, American republications of foreign chemical works.

We now come, in the order of history, to the name of Prof. John Redman Coxe, who deserves mention for the part he played in inaugurating a movement, which, as we shall see, has contributed, perhaps, more than any other to the progress of Medical Chemistry in the United States. A part of his medical education was obtained in the University of Edinburgh, but he graduated in the University of Pennsylvania in 1794. He afterwards spent considerable time in London, Edinburgh, and Paris. In 1809, he was elected by his Alma Mater Professor of Chemistry, and was transferred to the chair of *Materia Medica* in 1818. While in this latter chair he was the "leading spirit" in a movement to provide a special course of lectures in Pharmacy for the young druggists and druggists' clerks of Philadelphia. This was early in 1821. This movement arrested the attention of the leading druggists of the city, and led



them at once to establish a new and independent institution—first called the College of Apothecaries, but changed the next year to the Philadelphia College of Pharmacy—to secure the same results, but upon a more liberal plan.

The founders of this college were wise men, and secured for their new institution professors of high scientific character. The first course of lectures was given in 1821–2. Dr. Samuel Jackson, a medical graduate of the University of Pennsylvania, was the first Professor of *Materia Medica*. In 1827 he was elected to a professorship in his Alma Mater. His career as a lecturer, as an author, and as a practitioner, was in all respects distinguished. Dr. Gerard Troost, afterwards eminent in other departments of science, was the first Professor of Chemistry, but was succeeded within a year by Dr. George B. Wood, happily still living to enjoy the rewards of a life well spent in the service of science and of humanity. His published works, at once so complete and scholarly, have honored the profession of which he has so long been a distinguished member.

In 1831, Dr. Wood was transferred to the department of *Materia Medica*. His successor in the chair of Chemistry was Dr. Franklin Bache, a worthy descendant of the eminent statesman and philosopher whose name he bore. In 1833, Professors Wood and Bache published the first edition of the *United States Dispensatory*, a work which has passed through thirteen (13) editions, and is still the indispensable handbook of the physician and pharmacist. These eminent professors impressed upon the College of Pharmacy a character for thorough science which it has never lost. Our brief sketch would be imperfect should we here fail to mention the name of the late Prof. William Procter, Jr., who became the Professor of Pharmacy in this college in 1846, and who by his scientific labors, prosecuted through many years, contributed more to the special department of Medical and Pharmaceutical Chemistry than, perhaps, any other American. It should here be mentioned that, four years after the establishment of the Philadelphia College of Pharmacy, its friends founded the *American Journal of Pharmacy*, a journal still issued, and which has contributed very greatly to the dissemination of a knowledge of chemistry in its relations to medicine.

The second College of Pharmacy in this country was established in New York in 1829, through the instrumentality of George D. Coggeshall, a graduate of the Philadelphia College. The first Professor of Chemistry was the late Dr. John Torrey, whose labors in science, and especially in American botany, have given him a name which will ever be honored:

## MEDICAL CHEMISTRY.

Having thus glanced at the history of the introduction of chemistry into our schools, in passing on to discuss the theme assigned us, MEDICAL CHEMISTRY, we find ourselves entering upon a broad domain of investigation. We might enlarge upon the many and wide bearings of chemistry upon medical practice, and show how indispensable it is to the best success of the practitioner; point out its grand achievements in the departments of physiology and pathology, and show how inseparable is its connection with the progress of medical science in all its departments;



but, perhaps, as more consonant with the occasion and with the limitations of the hour, we may restrict ourselves to a brief consideration of the more prominent of the *American Chemical Contributions to the Medical Progress of the Century*. In this review, we find that these contributions relate largely to the examination of the chemical and therapeutic properties of our indigenous plants.

One of the first of these plants examined was *Sanguinaria Canadensis*, or Blood-root. Attention was first called to this plant in 1803, by Dr. Wm. Downey, of Maryland, as a powerful emetic; and in 1819, Dr. Wm. Tully, of New Haven, investigated with care its therapeutic properties. In 1828, Dr. J. F. Dana, of Dartmouth, first chemically examined the plant, and succeeded in isolating a basic or alkaloidal principle which he called *Sanguinarine* (N. Y. Lyc. Nat. Hist., ii. 245, 1828). The identity in ultimate composition of this alkaloid with the alkaloid of *Chelidonium majus*, subsequently discovered by Probst and called *chelerythine*, was fully established by Dr. Joseph Schiel, of St. Louis, in 1865 (Amer. Journ. Sci. (2), xx. 220). A second principle was extracted from *Sanguinaria Canadensis* by Riegel, which he considered identical with Merck's porphyroxine, from opium; but this identity was subsequently denied by Dr. G. D. Gibb. A third proximate principle derived from this plant was described by Prof. E. S. Wayne, of Cincinnati (Amer. Journ. Pharm., 1856, 521); and for it Dr. Gibb proposed the name *puccine*. Prof. Wayne has also recognized in blood-root the presence of *chelidonic acid*, first found in the plant *Chelidonium majus*.

In 1819, Dr. John Torrey, while investigating a curious underground fungus called Tuckahoe or Indian-bread (*Scleroticum gigantum*), discovered a new principle which he termed *Sclerotine*, an account of which was read before the Lyceum of Natural History, New York, Nov. 15, 1819, and published in the N. Y. Med. Repository, Dec. 1820. In 1824 Braconnot described pectic acid, a principle now obtained from many succulent plants. In 1827 Dr. Torrey republished his former paper with additions, and showed the identity of the two substances (Amer. Journ. Sci. (2), xxvii. 439).

Another interesting native plant that early received attention is *Lobelia inflata*, known as Indian tobacco, and used as a medicine by the aborigines. The attention of the medical profession was first called to this plant by Rev. Manasseh Cutler, of Ipswich, Mass., eminent as a botanist in the latter part of the last century. *Lobelia* was first examined chemically in 1833 by Dr. S. Colhoun, Professor of Materia Medica in Jefferson Medical College, Philadelphia, who announced the existence of a basic principle capable of forming salts with acids, but failed to isolate the principle (Amer. Journ. Pharm., v. 300, 1833). Wm. Procter, Jr., who has already been referred to, in his Inaugural Thesis, in 1837, on *Lobelia inflata*, demonstrated that the active principle of the plant is a liquid alkaloid, which he succeeded in isolating. He named this principle *lobalina*, and he described the salt formed by it with the leading acids. His very elaborate thesis was published in the American Journal of Pharmacy for July, 1837. In November, 1850, Wm. Bastick read a paper before the Pharmaceutical Society of Great Britain on *Lobelia inflata*, in which he described the same alkaloid, and his name is often mentioned in foreign publications as its first discoverer. A number of cases of poisoning have occurred in this country from the use of this plant, chiefly as administered by empirics.

The next indigenous plant to be noticed is *Veratrum viride*, or Ameri-



can hellebore. This plant was known to the Indians chiefly as a poison. According to Joselin, an early visitor to this country, it was used by them in the selection of their chiefs, the individual found least susceptible to its effects being regarded as the "strongest of the party, and entitled to command the rest" (Amer. Journ. Pharm., vii. 203). It was brought to the attention of the medical profession about the year 1830, by Drs. Tully and Ives, of New Haven. Its therapeutic properties were more fully investigated by Dr. Charles Osgood, of Providence, in 1835 (Amer. Journ. Med. Sci., xvi. 296). In 1851 Dr. W. C. Norwood, of South Carolina, again brought it before the profession in a series of papers highly extolling its medicinal virtues.

The chemical history of this plant presents some features of peculiar interest. Very contradictory conclusions have been reached by different investigators in regard to the exact chemical nature of its active principle or principles. The first chemical examination of this plant was made in 1835 by Dr. Charles Osgood, but he failed to obtain satisfactory results (Amer. Journ. Pharm., vii. 202). It was again examined by Dr. Thos. R. Mitchell in 1837, who also failed to determine the true nature of its active principle (Ibid., ix. 181). After a somewhat extended examination, Henry W. Worthington, in 1838, concluded that the plant contained an alkaloid identical with *veratria*, previously obtained from *veratrum album*, its European congener (Ibid., x. 89). In 1857, Dr. Jos. G. Richardson, after a very elaborate investigation and an extended series of parallel chemical experiments, with the alkaloids of both these plants, came to the same conclusion (Ibid., 1857, 204). In 1862 Mr. G. J. Scattergood announced that in addition to the alkaloid *veratria*, the plant contained a resin, to which he ascribed the sedative action of the drug, and he also obtained some evidence of the probable existence of the alkaloid *jervia* in the plant (Proc. Amer. Pharm. Assoc., 1862). Mr. Charles Bullock, of Philadelphia, in 1865, claimed that the alkaloid in question was not identical with *veratria*, and that the resin of Scattergood owed its activity to the presence of another alkaloid. These principles were afterwards named respectively *veratroida* and *viridia* (Amer. Journ. Pharm., 1865, 321). In 1872 Dr. Eugene Peugnet, of New York, also assented to the want of identity between *veratroida* and *veratria*, and he announced the identity of the *viridia* of Bullock with the alkaloid *jervia*, first discovered in *veratrum album* by Simon (Med. Record, May, 1872). These views of Dr. Peugnet were endorsed by Mr. C. L. Mitchell, of Philadelphia, after an elaborate investigation in 1874 (Proc. Amer. Pharm. Assoc., 1874, 436). Lastly, in this singular history, in a paper in the January number of the American Journal of Pharmacy for the current year, it is again claimed that the alkaloid, other than *jervia*, of this plant is identical with *veratria*, it fully responding to all the known tests for this alkaloid. The paper just cited, by Dr. T. G. Wormley, also points out the behavior of *jervia* with reagents, and cites cases in which both alkaloids were recovered from the blood of animals poisoned with *veratrum viride*.

In 1875 Mr. Charles Bullock contributed a valuable paper on the methods of preparation and properties of *jervia* (Amer. Journ. Pharm., 1875, 449). In this connection we should not fail to mention the interesting and valuable series of experiments upon the physiological action of the alkaloids of this plant by Prof. Horatio C. Wood, Jr., of Philadelphia, published in the American Journal of the Medical Sciences, January, 1870, and the Philadelphia Medical Times, vols. ii. and iii.



Leaving this protracted notice of the American bellebore, let us turn to a plant of milder name and properties, the Wax Myrtle or Bayberry, the *Myrica cerifera* of the botanists. In 1819 the berries of this plant were examined chemically by Dr. J. F. Dana, then chemical assistant in Harvard University (Amer. Journ. Sci., i. 294). Mr. G. E. Moore, in 1862, made a complete analysis of the Wax of the Bayberry, and found it to consist of *palmitin* and *palmitic acid*, with a small quantity of *lauric acid* (Ibid. (2), xxxiii. 313). In 1863 the bark of the root of this plant was examined by Mr. Geo. M. Hambright, of Philadelphia, who found that it contained a new crystallizable principle, to which he gave the name *myricinic acid* (Amer. Journ. Pharm., 1863, 193). The bark of this plant, as a remedial agent, was first brought to the attention of the profession in 1822, by Dr. W. M. Fehnestock, of Harrisburg, Penn.

According to Rev. F. Heckewelder, the Indians of this country employed *Podophyllum peltatum*, or May apple, as a poison to destroy themselves (Eberle's Therapeutics, i. 205). This plant was long used as a popular cathartic, and was brought to the attention of physicians, by Dr. Bigelow, about 1818.

The first chemical examination of this plant was made in 1831, by Wm. Hodgson, who obtained a crystallizable bitter principle, which he believed to be the active principle of the plant, and which he named *podophyllin* (Amer. Journ. Pharm., iii. 273); but Prof. T. F. Mayer was led to believe that the principle obtained by Hodgson was the alkaloid *berberina* (Ibid., 1863, 98); and this fact was fully established by Prof. J. M. Maisch (Ibid., 303). After an elaborate examination of the plant by John R. Lewis, the results of which he presented as an Inaugural Essay, he concludes that the active properties of the root are due to the presence of two peculiar resinous principles, the one soluble, the other insoluble, in ether (Ibid., 1847, 165). According to Prof. Mayer, the root contains, besides berberina, a colorless alkaloid, a neutral volatilizable principle, and saponine (Ibid., 1863, 98).

A native plant that has received considerable attention at the hands of the physician and chemist is *Hydrastis Canadensis*, or Yellow puccoon. It was known both as a medicine and as a dye to the aborigines of this country, and employed by irregular practitioners before being used by the regular profession. The first chemical examination of this plant was made in 1851, by Alfred A. B. Durand, of Philadelphia (Am. Journ. Phar., 1851, 112). He obtained a colorless crystallizable base, which he named *hydrastia*, but he failed to obtain it in a pure state. In 1862, Mr. J. D. Perrins, of Worcester, England, obtained it pure and determined some of its properties. He read his paper before the London Pharmaceutical Society, April 2, 1862, an abstract appearing in the Chemical News (v. 204), and the paper in full in the London Pharmaceutical Journal for May, 1862. In 1863, F. Mahla, of Chicago, Illinois, in a very valuable paper published in Silliman's Journal (op. cit. (2), xxxvi. 57) very fully describes the properties of hydrastia and gives its ultimate composition. We have given the history of this alkaloid somewhat in detail, since there have been different claimants for the honor of its discovery.

Mr. F. Mahla, in 1861, fully established the presence of *berberina* in the *hydrastis Canadensis* (Sill. Journ. (2), xxxiii. 43). This was the first instance in which this alkaloid—now known to be so widely distributed in plants—was found in a plant belonging to the Ranunculaceæ, and it thus established the fact that the same alkaloid may occur in plants belonging to different families. The chemical history of the alkaloid

berberina is somewhat remarkable. In 1826, Chevallier and Pelletan discovered it in the bark of *Xanthoxylum clava Herculis*, and named it *xanthopierite*. In 1835, it was found as *berberina*, by Buchner, in *Berberis vulgaris*. These observers erroneously regarded it as a weak acid. Fleitman established its basic character; and Perrins, in 1862, showed the identity of xanthopierite with berberina, and established its formula. The probable existence of a third alkaloid in *hydrastis canadensis*, "more resembling berberina than hydrastia, but decidedly different from the former," was announced in 1873, by A. K. Hall, of Ann Arbor, Mich. (Am. Journ. Phar., 1873, 247). This third principle was more fully examined in 1875, by John C. Burt, of the University of Michigan (Ibid., 1875, 481).

*Cimicifuga racemosa*, or Black snakeroot, a native of the United States, was first introduced to the attention of the regular profession by Dr. Thos. J. Garden, of Charlotte, Va., in 1823. This plant was examined chemically in 1834, by John H. Tilghman (Amer. Journ. Phar., vi. 14); in 1843, by J. S. Jones (Ibid., xv. 1); and in 1861, by Geo. H. Davis (Ibid., 1861, 391); but neither of these gentlemen succeeded in obtaining the active principle of the plant. At a meeting of the N. Y. Academy of Medicine, April 3, 1871, Dr. S. R. Percy exhibited a sample of a new alkaloid obtained by him from the *cimicifuga racemosa*, which he named *cimicifugia* (Amer. Med. Times, N. Y., April, 1861).

The poisonous nature of the leaves of *Prunus Virginiana*, or Wild cherry, has long been known. As early as 1806, Dr. Coxe, of Philadelphia, conjectured that the poisonous properties of water distilled from the leaves of this plant were due to the presence of prussic acid (see Am. Journ. Pharm., 1859, 433). In 1834, Stephen Procter determined the proximate composition of the bark of the tree, and established the presence of hydrocyanic acid and a volatile oil, as products of distillation with water (Amer. Journ. Pharm., vi. 8). In 1838, Prof. Wm. Procter, Jr., established the existence of *amygdaline* and of a decomposing agent, identical with *emulsine*, in the bark, leaves, and kernels of the wild cherry, and showed that these principles (as had before been shown by Liebig and Woehler in the case of bitter almonds) were the source of the volatile oil and hydrocyanic acid obtained by distillation (Ibid., x. 197).

In 1856, Prof. E. S. Wayne, of Cincinnati, obtained from the root of *Leptandra Virginica*, or Black root, a peculiar, bitter, crystallizable principle, which possessed the properties of the plant, and which has been named *Leptandria* (Amer. Journ. Pharm., 1856, 510). Prof. Wayne also found that the root contained mannite (Ibid., 1859, 557). In 1863, Prof. F. F. Mayer announced the presence in the plant, of a glucoside closely resembling senegin in its properties, but more readily decomposed by alkalis (Ibid., 1863, 298).

We may next notice *Rhus toxicodendron*, or Poison oak, a native plant well known from its peculiar action upon the skin of some individuals. It was used by the Indians, both as a poison and as a medicinal agent. The first chemical examination of this plant seems to have been made in 1857, by Dr. Joseph Khittel, of Munich, who determined its principal proximate constituents, among which he claimed to have obtained a volatile alkaloid upon which the poisonous properties of the plant depended; but of this he failed to give any proof. In 1865, Prof. John M. Maisch, of Philadelphia, obtained from the fresh leaves of the plant, a new volatile, organic acid, which he named *Toxicodendric acid*, and fully



established that it was to the presence of this principle the plant owed its peculiar poisonous effects. Prof. Maish failed to obtain any evidence of the presence of a volatile alkaloid (Proc. Amer. Pharm. Assoc., 1865, 166). Several cases of poisoning of children who have eaten the fruit of this plant, have been reported.

The beautiful climbing plant *Gelsemium sempervirens*, or Yellow jasmine, a native of the South, was brought to the notice of the profession by an accident, in which a decoction of the root was administered for that of another plant. Its claims as a therapeutic agent were strongly urged upon the profession by Prof. Wm. Procter, in 1852 (Amer. Journ. Pharm., 1852, 307). This plant is now not only used quite generally by the profession of this country, but has found favor with the profession of Europe, having been first employed there more especially as a remedy for neuralgia. Its physiological effects were very carefully studied by Prof. Bartholow, of Cincinnati, in 1870 (London Practitioner, Oct. 1870); and very recently by Drs. Ringer and Murrell, of University College, England (Lancet, March and April, 1876). The first attempt to determine the chemical composition of the root of this plant was made in 1854, by M. H. Kollock (Amer. Journ. Pharm., 1855, 197). It was again examined in 1868, by C. L. Eberle (Ibid., 1869, 35). Both these gentlemen, however, failed to isolate the active principle. In 1869, Dr. T. G. Wormley obtained from the plant a new alkaloid, *gelseminia*, and an organic acid, *gelseminic acid*, the properties of both of which he fully described in the American Journal of Pharmacy for January, 1870. This paper also contains a report of a case of poisoning by the fluid extract of the plant, in which the alkaloid was recovered some months after death. On physiological grounds, Drs. Ringer and Murrell are inclined to the view that the plant contains two active principles, one capable of paralyzing, the other of exciting, the spinal cord.

An indigenous plant, used more especially as a domestic remedy, that early received chemical attention was the Prickly ash, *Xanthoxylum fraxineum*, which was examined in 1829, by Dr. Edward Staples, who found that it owed its active properties to the presence of a peculiar crystallizable principle which he named *xanthoxyline* (Amer. Journ. Pharm., i. 163). After the discovery of berberina and its identity with xanthopicrotine had been shown, it was generally believed that Dr. Staples's xanthoxyline was identical with berberina, especially when the wide distribution of this alkaloid became known; but Mr. Perrins, who first pointed out the identity of the two former alkaloids, states that xanthoxyline is an entirely distinct principle (Amer. Journ. Pharm., 1863, 459, note).

In connection with this early contribution of Dr. Staples may be mentioned that of Dr. J. F. Dana, who in 1819 discovered the existence of the animal alkaloid *cantharidine* in the Potato fly, *Lytta vittata*, the alkaloid having been first obtained in 1812 by Robiquet from the Spanish fly, *L. vesicatoria*. Other American contributions to the chemistry of cantharidine have been made by Prof. Procter, in 1852; by Wm. B. Warner, of Maryland, in 1856; and by Prof. Maisch, in 1872.

A stately American tree, named from its large and beautiful flower, the Tulip tree or *Liriodendron tulipifera*, affords a bark which was recommended to the profession by Dr. Young, of Philadelphia, in 1792, as a substitute for Peruvian bark in intermittent fevers, and in diseases requiring a gentle stimulant and tonic. In 1831, Prof. Emmet, of the University of Virginia, obtained from this bark a neutral, bitter principle

which he named *Liriodendrin*, and which he described as a white crystallizable solid (Amer. Journ. Pharm., iii. 5).

*Apocynum cannabinum*, or Indian hemp, long known as a powerful emetic and cathartic, was examined chemically by Dr. Knopp, who found it to contain, among other proximate constituents, a peculiar, bitter, active principle to which he gave the name *apocynin*. This plant was subsequently examined by Dr. Griscom (Amer. Journ. Med. Sci., May, 1836). This plant is different from *Cannabis indica*, also popularly known as Indian hemp, which was examined chemically in 1865, by Prof. Wm. Procter (Amer. Journ. Pharm., 1865, 23).

The American water hemlock, *Cicuta maculata*, found abundantly throughout the United States, was examined in 1855, by Jos. E. Young, who found it to contain a peculiar acid (probably the *conic* acid of Perschier), and the volatile alkaloid *conine*, first obtained from conium maculatum, by Geiger, in 1831.

Wahoo, *Euonymus atropurpureus*, so well known throughout the Western States, and sometimes called "burning bush," from the brilliancy of its crimson fruit, was made the subject of a very elaborate chemical examination by Wm. F. Wenzell, in 1862, who found it to contain a peculiar basic principle, which he named *Euonymine*, and a new organic acid, *euonic acid* (Amer. Journ. Pharm., xxxiv. 387).

Many other American plants have contributed to the wants of the physician, and have been the subjects of chemical examination, but special reference to them is necessarily omitted.

We now come to consider the history of the discovery of a compound which is not only interesting in itself, but is more especially so on account of its subsequent applications and the important position it now holds in the medical world.

In 1831, Dr. Samuel Guthrie, of Sackett's Harbor, N. Y., a man of unusual chemical knowledge for his time, discovered a substance which he prepared by distilling a mixture of chloride of lime and alcohol, and an account of which he published in the American Journal of Sciences, Oct. 1831, under the title "A new mode of preparing a spirituous solution of chloric ether." In this paper Dr. Guthrie states that in order to ascertain the effect of this substance in full doses on the healthy subject, and thus discover its probable value as a medicine, he had, during the last six months, administered it to a great number of persons, not only very freely, but frequently to the point of intoxication, and that the effects were grateful both to the palate and the stomach, and he concluded that "it would seem to promise much as a remedy in cases requiring a safe, quick, energetic, and palatable stimulant." His attention was, as he states, first directed to this subject by a statement in Prof. Silliman's Elements of Chemistry (vol. ii. p. 20), then just published, to the effect that an alcoholic solution of chloric ether, when diluted, was a grateful diffusible stimulant and might probably be introduced in medicine.

Prof. Silliman distributed samples of this substance to Dr. Eli Ives, of the Medical Department of Yale College, and to others, to be used in their practice. Under date of January 2, 1832, Dr. Ives reported that he had administered it in a number of cases with marked advantage, and had also used it by inhalation with good results (Amer. Journ. Sci., xxi. 406). The product thus produced by Dr. Guthrie was regarded by him at the time as the substance then known as "chloric ether" or "Dutch liquid," whereas it was an entirely new and distinct substance, that now



known as *chloroform*. Chloroform was also discovered by Soubeiran, of France, and an account of it published in February, 1831, under the name of *Ether bichlorique*. So, also, Liebig, in 1832, made another independent discovery of the same substance, naming it *Chloride of carbon*. It was named chloroform by Dumas, who discovered its true chemical constitution in 1834. A committee of the Medico-Chirurgical Society of Edinburgh awarded Dr. Guthrie the credit of having first published an account of its therapeutical effects as a diffusible stimulant in 1832 (*Amer. Journ. Sci.* (2) vii. 143).

As this substance afterwards became a prominent agent in producing anaesthesia, it leads us naturally, but very briefly, to notice the use of this and other substances inhaled for anaesthetic purposes, and the part which Americans have taken in a discovery which has proved an inestimable blessing to mankind.

In this memorial year, we naturally follow the years back to the beginning of the century we commemorate, and find that in 1776, or just one hundred years ago, Dr. Priestley, who had previously made the brilliant discovery of oxygen, discovered *Nitrous Oxide*, which he called *Dephlogisticated Nitrous Air*. In 1779, Sir Humphry Davy, then a very young man, entered upon a series of experiments in Bristol with this nitrous air, which he named nitrous oxide, and on the 11th of April of that year, made the first inhalation of the gas, and recorded its effects upon himself. By his investigations he ascertained its exhilarating effect, and discovered its power, when inhaled, to remove intense physical pain. His remarkable generalization from his experiments was expressed in the following oft-quoted words: "As nitrous oxide in its extensive application appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place." (*Researches, etc., concerning Nitrous Oxide and its Respiration*, Bristol, June, 1800.) While this suggestion appears to have been forgotten, yet nitrous oxide became widely known and used as a stimulant, and its administration as "laughing gas" was a matter of popular exhibition. In like manner, ether, the date of the first inhalation of which is in some obscurity, was used for the same purpose in the United States, as mentioned by the earlier writers on chemistry. In the experiments with both nitrous oxide and ether, there were cases in which these agents produced perfect insensibility, but the anaesthetic condition was not specially observed.

In the fall of 1844, Horace Wells, a dentist of Hartford, having witnessed an exhibition of the inhalation of nitrous oxide, and observed that a person under the influence of the gas was injured without being conscious of suffering, boldly inhaled the gas, and had a tooth removed without sense of pain, and gave it to others for the same purpose, with similar results. Thus the suggestion of Sir Humphry Davy in Bristol, England, published in 1800, was realized by Horace Wells at Hartford, Conn., in 1844.

In 1846, Wm. T. G. Morton, a dentist of Boston, a former student of Wells, and aware of his labors with nitrous oxide, commenced experiments with ether for the same end. The administration, in the Massachusetts Hospital, of ether by inhalation to a patient upon whom the eminent Dr. John C. Warren performed a surgical operation, authenticated it as an anaesthetic agent to the surgical and medical profession, and from that time the knowledge and practice of anaesthesia extended rapidly over the world.

As already shown, chloroform was employed by inhalation by Dr. Ives, of New Haven, in his practice in the winter of 1831-32 with marked benefit. In March, 1847, M. Flourens experimented with this agent upon lower animals, and in November of the same year the distinguished Prof. James Y. Simpson, of the University of Edinburgh, employed it as an anæsthetic agent with success, and introduced it into surgical and obstetrical practice.

Thus, in summary, we find that anæsthesia, first suggested by Sir Humphry Davy, in 1800, was demonstrated with nitrous oxide as an agent, by Horace Wells, in 1844; with ether as an agent, by Wm. T. G. Morton, in 1846; and with chloroform, by Sir James Y. Simpson, in 1847.

The next American chemical contribution to medicine that we may mention, is that on the "Origin of Urea in the Body," by Prof. John C. Draper, of the University of the City of New York (*New York Journal of Medicine*, Feb. 1856). In this paper the author shows the error in the statement of Liebig that muscular action increases the amount of urea secreted. The process employed was the decomposition of urea by nitroso-nitric acid, and weighing the carbonic acid produced as carbonate of baryta. The results obtained by Prof. Draper have since been verified by Fick and Wislicenus, but the credit of the first disproof of the statement of Liebig belongs to Dr. Draper.

Dr. Draper has also contributed papers, which may be mentioned in this connection, on "Products of Respiration," *New York Med. Times*, July, 1856; "Insensible Perspiration," *Proceedings of the New York Academy of Medicine*, May, 1864; "The Heat produced in the Body, and the Effects of Exposure to Cold," *American Journal Science and Arts*, Dec. 1872.

The last contribution we shall mention in this connection, is a valuable paper in the department of Physiological Chemistry, entitled "Experimental Researches into a new Excretory Function of the Liver," by Professor Austin Flint, Jr., widely known in the field of experimental physiology. This paper was published in the *American Journal of the Medical Sciences* for October, 1862; and afterwards presented to the French Academy of Sciences, from which it received in 1869 honorable mention and an award of 1500 francs. The important discoveries put forth in this memoir were the production of cholesterine in the physiological wear of the brain and nervous tissue, and its elimination by the liver, and discharge from the body in the form of stercorine. Dr. Flint's researches and interesting conclusions upon this subject have lately been confirmed in Germany, by experiments in which cholesteramia has been produced in animals by injection of cholesterine into the blood.

## TOXICOLOGY.

We now enter upon the other and not less important branch of the subject assigned us, namely that of TOXICOLOGY. This science is one of the highest moment to the race. While health and life are assailed by various diseases, by the ill-adjustment of outward circumstances, such as climate, locality and the like, by the unsuitableness of food and drink, or by an excessive use of these, and by a thousand other harmful conditions, these



assaults are generally made by slow and noticeable approaches, and are within the ken of the physician. But there have always lurked in the mineral and organic kingdoms, foes which may be likened to assassins who spring upon the unwary and destroy life as by a secret blow. These assailants are the poisons, the very Thugs of nature.

Before the present century little was known of poisons beyond their deadly effects and the attending physiological circumstances. Indeed, any true knowledge of poisons was unattainable until the advent of Chemistry as an exact science. Poisons are naturally grouped into two kinds—inorganic and organic.

In noticing the inorganic or mineral poisons, that one which holds the highest position in historical toxicology, and the one which until recently has been used as a toxic agent very much more than any other, is *Arsenic*. Although known in its metallic state, and as arsenious acid, as early as the eighth century, to Geber, the Arabian, and although it had been used as a poison for centuries, yet so little progress had been made in regard to its chemical detection under these circumstances, that Sir R. Christison, as late as 1824, declared that the tests for arsenic at that time in general use were so fallacious, when applied to complex mixtures, as to be unfit for medico-legal investigations. He then proposed a process for the detection of this metal which, as modified by Fresenius and Babo, continues in use to the present day. At the time of introducing this method, Prof. Christison remarked that by it he was able to detect the one-sixteenth of a grain of the poison. This, at the time, was regarded as a great triumph of analytical skill. Not long before this (1795) Dr. Black stated that one grain was the least he could detect; and at a somewhat earlier period, yet less than a century since (1786), Hahnemann stated that ten grains was the least quantity he could recover.

In 1836, Mr. Marsh, of Woolwich, England, proposed for the detection of this metal, a method which has since been known by his name, and which has proved of the highest value in chemico-legal practice. As originally employed by Mr. Marsh, this test was restricted to obtaining deposits of the metal from the ignited jet of the arsenide of hydrogen; but in 1841 Berzelius proposed the reduction of the arsenical gas by heat applied to the exit tube of the apparatus, and it has been found that this method is even more delicate than that proposed by Marsh. In 1841 Dr. Hugo Reinsch proposed, for the detection of this metal, his copper test, which has proved a most admirable method for the recovery of the poison, especially from complex organic mixtures. In point of delicacy, as now employed, this test is not inferior to the process of Marsh, and it has in certain cases even the advantage over the latter in simplicity of application. The two tests now mentioned, both in regard to simplicity of application and delicacy of reaction, leave little or nothing more to be desired in regard to the recovery and identification of this poison.

One of the first American contributions relating to the detection of arsenic was by Prof. James F. Dana, a graduate of Harvard University, who studied chemistry in London, and was afterwards Professor of Chemistry in Dartmouth College and in the College of Physicians and Surgeons, New York. As early as 1816, he prepared a paper on the "Tests for Arsenic," for which he received the award of the Boylston prize. In 1818, Dr. Thomas Cooper announced the use of chromate of potash as a test for arsenic; but it did not prove to be a distinctive test. In the same year, he read a paper on the subject before the American Philosophical Society (*Amer. Journ. Sci.*, iv. 16). In 1830, Prof. John

P. Emmet, of the University of Virginia, proposed iodide of potassium as a test for this metal. In the next year (1831) Dr. Lewis Feuchtwanger published a paper entitled "Remarks on Arsenic, with drawings of the color of its precipitates," in which he gave a full account of the processes then known for the detection of this poison (*Amer. Journ. Sci.*, xix. 339). An important and original contribution on this subject was made in 1832, by Prof. J. K. Mitchell, of Philadelphia. In this paper, "On the Properties of Arsenic," Dr. Mitchell determined the specific gravity of the different varieties of arsenious acid; its solubility under various conditions; and the vaporizing temperature of metallic arsenic and of arsenious acid (*Amer. Journ. Med. Sci.*, x. 126).

The next contribution to be mentioned is that "On the Detection of Arsenic in Medico-Legal Investigations," by Dr. Wm. R. Fisher, of the University of Maryland, in a paper read in 1836 before the Maryland Academy of Science and Literature, and published in their *Transactions* (vol. i. p. 117). In 1838, Dr. Robert B. Hall published a *Summary of Experiments upon dogs, with hydrated peroxide of iron as an antidote in arsenical poisoning* (*Amer. Journ. Pharm.*, x. 263). And in 1840, Dr. Fisher, already mentioned, contributed a paper on the same subject (*Ibid.*, xii. 1). In 1841, Prof. J. Lawrence Smith, of Louisville (to whom science is indebted for many original researches, and whose special investigations of meteoric bodies have given him a wide and lasting reputation), when a student in Paris, prepared a valuable paper *On the Tests and Antidotes for Arsenic* (*Am. Journ. Sci.*, 40, 278). Two years later (1843), Dr. D. P. Gardner, Professor of Chemistry in Hampden-Sidney College, Va., contributed an elaborate paper *On the Application of Reinsch's test for detecting Arsenic in Medico-Legal Investigations* (*Amer. Journ. Sci.*, 44, 240). In 1862, Charles H. Porter, Professor of Chemistry and Medical Jurisprudence, Albany Medical College, presented to the Medical Society of New York an excellent paper entitled *Medico-Legal Contributions on Arsenic*, which contains reports of a number of cases of arsenical poisoning, together with an account of the methods employed in their chemical examination.

We next notice a very valuable contribution by Prof. John C. Draper, of the University of the City of New York, *On the Quantitative Determination of Arsenic*, published in the *American Chemist* for June, 1872. Professor Draper suggests a modification of Marsh's apparatus, and the use of a ribbon of magnesium for decomposing the arsenical solution; and, also, the use of a fagot of platinum wire on which the arsenic forms a coating, the weight of which can be determined. By re-heating the fagot in dry oxygen, the arsenic is obtained in the form of oxide, which may be dissolved in water and submitted to the usual tests. In July of the same year, Dr. Draper published in the same journal a paper *On the Distribution of Arsenic in the Body*. Another contribution to this subject that deserves mention, is a record of *The Chemical Testimony in the Sherman Poisoning Case*, by Prof. George F. Barker, of the University of Pennsylvania (*Amer. Chemist*, June, 1872). This paper contains a detailed account of the methods pursued and results obtained in the examination of the different tissues submitted for analysis. In this case, a quantity of arsenic, corresponding to about five grains for the entire organ, was obtained from a portion of the liver. The bodies of four (4) of the eleven (11) persons supposed to have been poisoned by Mrs. Sherman were examined by Prof. Barker, and arsenic found in each.



Having thus noticed the principal American contributions relative to arsenic, it is proper in this connection to refer to some of the more important American contributions relating to other poisons.

In 1827, Prof. Robert Hare proposed a method for determining the presence of opium by the reaction of one of its constituents, meconic acid, in striking a red color with a persalt of iron. He asserted that this test would show the presence of laudanum when only ten (10) drops were contained in one-half gallon of water (*Amer. Journ. Sci.*, xii. 290). With but little modification this test is the one employed at the present time for the detection of opium.

In 1856, Dr. Lewis H. Steiner, of Baltimore, made a report to the American Medical Association, On Strychnia, in which, in addition to a discussion of the chemistry of the subject, he gives a detailed history of the noted case of Dr. Gardner, of Washington, who destroyed himself with that poison. In a paper On the Chemical Reactions of Strychnia, published by Dr. T. G. Wormley, in 1859, in the American Journal of Science, the relative delicacy of the various tests for this poison is pointed out. The fact that the color-reaction of strychnine is interfered with by the presence of morphine, having first been noticed by A. W. Brieger in 1850, this interference is fully considered in this paper, and the conclusion reached, that the interference increases both with the relative proportion and absolute quantity of morphine in the mixture submitted to the test. Another paper to be mentioned in this immediate connection, is that of Prof. John J. Reese, On the Detection of Strychnia as a Poison, and the Influence of Morphia in Disguising the usual Color-test, published in the American Journal of the Medical Sciences for October, 1861. So also in this connection may be mentioned a valuable contribution On the Behavior of the Color-test for Strychnine, with other Vegetable and Animal Proximate Principles, by Dr. Thomas E. Jenkins, of Louisville, Ky. (*Semi-monthly Med. News*, April, 1859). The behavior of this test with a number of proximate principles other than strychnine, was first examined in 1856, by M. Eboli, Professor of Chemistry at the Academy of Medicine, Lima. Dr. Jenkins so extended this examination as to include about fifty of these principles; and Prof. Wm. A. Guy, of London, in 1861 investigated some sixteen additional substances.

Another contribution to this subject is a Report of a Trial for Poisoning by Strychnia, by Prof. Geo. F. Barker, recorded in the American Journal of the Medical Sciences for October, 1864. In this paper Prof. Barker gives a very complete history of a case remarkable in that violent symptoms were present in about three minutes after the poison had been taken by an adult, the effects thus manifesting themselves perhaps more rapidly than in any other instance yet reported of poisoning by this substance.

An elaborate paper entitled Experiments of Poisoning with Vegetable Alkaloids, by Dr. J. H. Salisbury, was published in the American Journal of the Medical Sciences for 1862. In regard to the limit of the reactions of poisons and other principles, with chemical reagents, Dr. T. G. Wormley has contributed papers on the reactions of the following: Atropine, *Chemical News*, London, June, 1860; Brucine, *Ibid.*, July, 1860; Morphine, *Ibid.*, Sept. 1860; Narcotine and Meconic Acid, *Ibid.*, Sept. 1860; Corrosive Sublimate, *Ibid.*, Sept. 1860; Veratrine, *Ohio Med. and Surg. Journ.*, vol. xii., No. 6; Nicotine and Daturine, *Ibid.*, vol. xiii., No. 1; Solanine, *Ibid.*, vol. xiii., No. 2; Codeine, Meconine,

Narcine, and Aconitine, *Ibid.*, vol. xiii., No. 4; Conine, *Ibid.*, vol. xiv., No. 1; Oxalic Acid, *Ibid.*, vol. xiv., No. 5.

Mention may next be made of a curious plant, *Erythroxylon coca*, the leaves of which have arrested considerable attention because of their use by the Indians of Peru for the purpose of producing excitement, and giving strength for prolonged physical exertion. Dr. Samuel R. Percy, of New York, presented a paper on this subject before the N. Y. Academy of Medicine, Dec. 2, 1857, and exhibited fine colorless crystals of the alkaloid of the plant, for which he proposed the name *Erythroxylene* (*Amer. Med. Times*, Nov. 1860). In 1860 Prof. Woehler and Dr. Niemann, of Gottingen, obtained the same alkaloid, giving it the name *cocaine*.

In 1866, Dr. Percy, of New York, presented a paper to the American Medical Association, On Digitaline, its Chemical, Physiological, and Therapeutic Action, for which the Association awarded a prize; and, in 1868, the same gentleman received a prize from the Alumni Association of the Medical Department of Columbia College for a paper On Atropia, its Chemical, Physiological, and Therapeutic Action, with Experiments instituted to ascertain its Toxicological Properties. In January, 1871, Prof. John J. Reese, of Philadelphia, published a communication On the Antagonism of Poisons, in the *American Journal of the Medical Sciences*, in which he examined the antagonism of morphia with hydrocyanic acid, atropia, strychnia, aconitia, and arsenic, and also of strychnia with tobacco, aconite, iodine, and Calabar bean. For the destruction of the organic tissues, in searching for poisons in medico-legal investigations, Prof. Henry Wurtz, in 1851, proposed the use of bromine as an agent possessing certain advantages over the ordinary agents used for this purpose (*Silliman's Journal* (2), xi. 405).

We now notice a very interesting and valuable paper on Experimental Researches relative to Corroval and Vao, two new varieties of Woorara, the South American Arrow Poison; by Drs. Wm. A. Hammond and S. Weir Mitchell, published in the *American Journal of the Medical Sciences*, July, 1859. This is an original and exhaustive examination of the physiological effects, and the chemical properties and physical characters, of these varieties of Woorara. The authors extracted from both varieties an alkaloid, for which they proposed the name *corrovalia*, obtaining it in larger quantity from the variety corroval. This substance was not obtained in a crystalline state, nor were any of its salts. One of the authors of the last-named paper, Dr. S. Weir Mitchell, published in the *Smithsonian Contributions*, vol. xii. (1860), a very elaborate and complete monograph, entitled, *Researches upon the Venom of the Rattlesnake*. This contribution is marked by the same patient and thorough research which characterizes the other scientific labors of this original investigator. It considers the anatomy of the venom apparatus, the physiological mechanism of the bite, the toxicological action of the venom on warm-blooded animals, and the various antidotes for the poison. His chemical investigations show the toxicological element of the venom to be a peculiar albuminoid principle, which he names *crotaline*.

Again, in 1868, Dr. Mitchell instituted a series of experiments on the Insusceptibility of Pigeons to the Toxic Action of Opium, in which he showed that this bird was almost wholly insusceptible to the action of that drug. The same immunity was observed whether the drug itself, or morphia, was employed, and also whether it was administered internally or employed hypodermically. In his final experiment, Dr. Mitchell



administered to a large pigeon twenty-one grains of powdered opium, without producing any evidence of opium poisoning (*Amer. Journ. of the Med. Sci.*, Jan. 1869). Dr. B. W. Richardson, of London, on repeating Dr. Mitchell's experiments, fully confirmed his results. As a comparison of the relative susceptibility of the pigeon and the child, Dr. Richardson states that a pigeon can receive at once as much opium as would produce dangerous or even fatal symptoms, if divided equally and administered to twenty children under one year old, the weight of the bird being two hundred times less than the combined weight of the children (*Brit. and For. Med. Chir. Rev.*, April, 1869). Continuing his researches, Dr. Mitchell extended his experiments to the physiological effects of the derivative alkaloids of opium, including morphia, narcotina, thebaia, meconine, codeia, narceia, and cryptopia, employed both internally and subcutaneously. In these experiments, Dr. Mitchell obtained some very interesting and novel results. Thus, he found that while opium, which is a poison to man, is with difficulty hurtful to the pigeon; on the other hand, narcotina, which is nearly inert in man, is fatal to birds (*Amer. Journ. of the Med. Sci.*, Jan. 1870).

We next notice some very original and interesting investigations of Dr. James Blake, of San Francisco, who has been engaged for many years in examining the connection between Isomorphism, Molecular Weight, and Physiological Action (*Amer. Journ. Sci.* (2) viii. p. 193). Dr. Blake has investigated the effects of compounds or salts of forty (40) of the elements, including substances contained in all the more important isomorphous groups, and in all of these, with the exception of the compounds of potassium and ammonia, finds that when introduced directly into the blood of living animals, the substances in the same isomorphous group exert analogous effects; and also that amongst the more purely metallic elements, the intensity of physiological action is in proportion to the atomic weight of the substance compared with other substances in the same isomorphous group. From experiments made by others, Dr. Blake believes that the same law will apply to organic or carbon compounds, and that living matter will be found to be a valuable reagent for elucidating their molecular relations. His latest researches on Lanthanium and Didymium place the former evidently in the magnesium group and the latter with aluminium. These researches, with those of Drs. Crum Brown and Fraser, and with those of Dr. Richardson, are in a new field of inquiry, and promise very interesting and important results to science.

Having thus glanced at the more important American contributions to toxicology, the way is prepared to take a broader view of this science, and observe the progress of its development, especially in its chemical features. This progress will be seen to be greater in regard to the organic poisons, the marked advance in methods of chemical analysis having made such progress possible.

At the opening of the present century, the fact that the toxic effect of certain vegetable poisons was due to the agency of a peculiar active principle, resident in the plant, had not been determined. The vegetable substance in which the existence of a principle of this kind was first observed was opium, in which Sertürner and also perhaps Seguin in 1804 recognized the presence of a new substance; but it was not until 1817 that Sertürner obtained it in a pure state, and examined its properties. He found that the alcoholic solution of this new principle acted upon

vegetable colors like solutions of the mineral alkalies, and that the substance combined directly with acids, forming neutral salts which were soluble in water, and that it was precipitated from solutions of its salts by the mineral alkalies. To this substance Sertürner gave the name *morphine*, and from the properties just mentioned he regarded it as a kind of alkali; hence the name *vegeto-alkali* or *alkaloid* for principles of this kind.

Very soon after the discovery of *morphine* it was found that *nux vomica*, white hellebore, *cinchona* bark, *belladonna*, tobacco, and certain other vegetable products which had been long known as capable of exerting marked physiological effects, owed their activity to the presence of similar alkaline principles. The number of such natural principles now known is quite considerable. Since 1848 a great number of organic alkalies have been obtained artificially, some of which rival potash and soda in the degree of their alkalinity. The study of these artificial alkaloids has thrown much light upon the constitution of the natural alkaloids, which is, as yet, imperfectly understood.

The discovery of the natural alkaloids has been of great service to the physician, giving him a more concentrated and manageable form of medicine; but to the toxicological chemist this discovery has been of the very highest value, enabling him in cases of poisoning by crude vegetable substances, in just so far as he can recover the alkaloid or active principle from complex mixtures (such as the contents of the stomach), and can separate and determine it by special chemical properties, to identify the toxic substance employed. There are, however, many vegetable and animal poisons, the exact nature of the active principle of which has not yet been determined.

Formerly, about the only method of detecting vegetable poisons was by means of the physical and botanical characters of the substance taken, such as the leaves, seeds, etc., and this method is yet of service in furnishing corroborative evidence in cases even in which the nature of the peculiar principle is known. It is obvious that in poisoning by crude vegetable and animal substances, we can determine the presence of the poison by chemical methods only, first, when we know that the substance contains an alkaloid or other principle peculiar to itself; second, when we are able to recover this principle from complex mixtures; and third, when we are acquainted with one or more chemical reactions characteristic of this principle. Thus, in poisoning by opium, we cannot prove the existence of opium as a whole, but only inferentially, by proving the presence of a principle peculiar to this drug. Our success in the discovery of organic poisons, where the existence of a peculiar principle is already known, depends largely on our ability to recover such principle from complex mixtures in a state sufficiently pure for the application of special tests.

It was not until 1851 that any real progress was made in this direction, when Prof. Stas, of Brussels, introduced a systematic method for such recovery. This method has proved of the highest importance, and marks an era in toxicological science. It is based upon the fact that the salts of the alkaloids, as a class, are soluble in water and alcohol, but are insoluble in ether; and that these salts when in solution are readily decomposed by the mineral alkalies with the elimination of the alkaloids, which in their free and uncombined state are more or less readily soluble in ether. In any given case therefore, in so far as the active principle or alkaloid



is soluble in ether, and this liquid fails to extract foreign animal and vegetable matter, in just so far can we obtain the alkaloid in its pure state. Professor Stas successfully applied his method for the recovery of the principal alkaloids likely to be met with in chemico-legal investigations, employing for this purpose the usual extracts of the plants in which they are found. Professor Otto, of Brunswick, proposed to modify the method of Stas, in the case of the fixed alkaloids, by first washing the acid aqueous solution of the alkaloidal salt with ether as long as this fluid was colored; the solution is then rendered alkaline and the liberated alkaloid extracted with ether as before proposed. Professor Otto claimed, and justly, that in this manner the alkaloid might be obtained in a state of greater purity, and almost invariably in a crystallized condition.

In 1853, Professors Graham and Hoffman, of London, proposed a method for the recovery of strychnine from organic mixtures, which was afterwards extended to other alkaloids; it is based upon the fact that when a solution of strychnine in its free state is agitated with charcoal, the charcoal absorbs the poison and yields it up to boiling alcohol (Quart. Journ. Chem. Soc., 1853). In practice, in chemico-legal investigations, this method is inferior to that of Stas. In 1856, Messrs. Rogers and Girdwood, of London, proposed the use of chloroform instead of ether, as advised by Stas, for the extraction of the alkaloids. They also proposed to destroy the last traces of foreign matter by charring the chloroform residue with concentrated sulphuric acid over a water-bath (Lancet, London, June, 1856). The use of chloroform as advised by these gentlemen has proved of value in researches of this kind, since it is a better solvent of most of the alkaloids than ether, and has therefore an advantage in certain cases; but, on the other hand, it has sometimes the disadvantage of taking up more freely than ether foreign animal and vegetable matters. Another method for the extraction of the alkaloids from complex mixtures is that of Usler and Erdmann, who proposed the use of amylic alcohol, the principle of the process being much the same as in the method of Stas. Amylic alcohol is especially adapted to the recovery of morphine, solanine, and certain other alkaloids, which are more or less freely soluble in this liquid, whereas they are but very sparingly soluble both in ether and chloroform, and therefore are but imperfectly extracted by these liquids.

In 1862, Professor Thomas Graham, of London, in his very important contribution on liquid diffusion, showed that moist organic membranes have the remarkable property of separating crystallizable substances when in solution from such as are uncrystallizable, the former readily passing through such membranes when surrounded by a liquid, whereas the latter fail to pass or pass only very slowly. These classes of substances he named respectively *crystalloids* and *colloids*, and to this method of separation he applied the term *dialysis*. This method is applicable to both inorganic and organic bodies, and is often found very useful in toxicological investigations.

The latest contribution to this department of research is that of Prof. Dragendorff, of the University of Dorpat, who, in 1868, proposed a very elaborate and exhaustive method for the extraction of the alkaloids and similar principles, and for their separation from each other, based upon their behavior with petroleum-naphtha, benzole, chloroform, and amylic alcohol, dividing them into several groups according as they are affected by these different liquids under certain specified conditions.

From this brief historical sketch, we learn that very considerable attention has been directed to this important and essential part of toxicological chemistry; and, it may be added, the results have been such as to leave little to be desired in regard to the recovery of a large number of organic poisons. We are now prepared to take a rapid survey of the progress made in regard to the special identification of poisons by chemical and other tests. Even less than a third of a century ago, there were but few of the organic poisons for which special and unerring tests were known, especially when present in the minute quantity usually met with in chemico-legal investigations.

In September, 1843, E. Marchand made the important discovery that if strychnine be treated with concentrated sulphuric acid containing a little nitric acid and peroxide of lead, it dissolves with the production of a series of colors peculiar to that alkaloid. The tests employed for the detection of this poison prior to the discovery of this color reaction, which has since been known as the color-test, gave reactions more or less common to substances other than strychnine. In fact, this color-test is the only one yet known the reaction of which, taken alone, is peculiar to strychnine. It was considered a marvel of delicacy of reaction when Marchand announced that this test would reveal the presence of a quantity of strychnine not exceeding the one-thousandth of a grain in weight. This test has since been modified by Mack, Otto, and others, by substituting for the nitric acid and lead compound other oxidizing compounds; and it will now, in the hands of a skillful manipulator, show the presence of strychnine when in quantity not exceeding, perhaps, the one-millionth of a grain.

The discovery of this test did much to stimulate chemists to search for special or characteristic tests for other alkaloids and vegetable principles likely to be encountered in chemico-legal investigations, and in many instances with success. Much remains, however, to be done in this direction, even in regard to some very well known poisons of this class. There are some poisons, the presence of which may be determined by what is known as a combination of tests, no one of which is in itself peculiar or exclusive; but there are others for which we have as yet neither peculiar and distinctive tests, nor any peculiar combination of tests for their detection, especially when present in minute quantity.

It is less than a quarter of a century since the aid of the *microscope* was, to any marked extent, invoked in this department of research, yet within this comparatively brief period its use has very greatly extended our means of determining the specific nature of the results of chemical tests. This instrument not only often enables us to determine the true nature of a precipitate or sublimate by its crystalline or other form, the character of which would otherwise be doubtful, but it enables us to recognize and identify certain substances when present in quantities so minute as to be far beyond the reach of the ordinary methods of examination. Thus by micro-chemical analysis we are able to identify with absolute certainty the reaction of the one hundred thousandth part of a grain of hydrocyanic acid, and of certain other poisons in quantity equally minute. Even a sublimate, consisting of a few crystals, each of which does not exceed the one hundred millionth of a grain in weight, may, under certain conditions, serve to characterize the presence of arsenic beyond a question of doubt. The chief contributors to the micro-chemistry of poisons have been Professors Guy and Taylor, the eminent



toxicologists of England; Drs. Helwig and Earhard, of Germany; and Professor Wormley, of the United States.

For the final purification and subsequent examination by means of the microscope either directly or under the action of reagents, the process of *sublimation* has been proposed, as applicable to both inorganic and organic substances. In 1858, Professor Wm. A. Guy, of London, called special attention to the process of sublimation for the detection of arsenic, corrosive sublimate, and certain other inorganic poisons; and in 1865, Dr. Helwig, of Mayence, announced that in like manner certain alkaloids and vegetable principles furnished sublimates, some of which were characteristic in their microscopic forms and in their behavior with reagents, and he gave photographic illustrations of many of the forms thus obtained. In 1867, Dr. Guy modified somewhat Helwig's method, extended it to a much larger class of objects, and proposed to add to the diagnostic value of the method by a simple arrangement for noting the temperature at which changes in form and color, and sublimation itself, occur.

The brilliant discoveries of Bunsen and Kirchhoff, in 1859, which enable us by means of *spectrum analysis* to recognize and identify with unerring certainty the elementary forms of matter and certain compounds, even when present in quantities so minute as to be far beyond the reach of the ordinary methods of analysis, have not been without some fruit in the department of chemico-legal investigations. Thus Dr. Benze Jones found by this method thallium in the liver, when the ordinary chemical tests failed to reveal its presence.

It is a proof of the great activity and sagacity displayed in modern science that the spectroscope with its amazing capabilities should so soon be combined with the microscope, an instrument of scarcely less capabilities, thus forming the *micro-spectroscope*, by which we are enabled to make new discoveries of the highest value in Medico-legal Chemistry. For this combination of the two instruments we are chiefly indebted to Mr. H. C. Sorby, who has with its aid determined the spectra of a large number of organic coloring principles when in solutions. One of the most important applications of this instrument thus far made in legal medicine, is that for the detection of blood, its delicacy being such as, according to Mr. Sorby, and as confirmed by our own observations, to reveal the presence of a single corpuscle, or less than the one thirteen millionth of a milligramme, or one five hundred millionth of a grain, of that fluid. Although this method will serve to discriminate the coloring matter of the blood from other coloring principles, yet it does not enable us to distinguish the blood of any one animal, including man, from that of another. This, however, can be done within certain limits, but only within certain limits, by means of the microscope; this instrument enables us to specify with great certainty certain animals, even of the same class, from which the blood was *not* derived, but it does not enable us to *positively individualize* the animal from which it *was* derived.

Our discussion of toxicology would be very incomplete without some notice of the subject of the *absorption* of poisons. Prior to the important discoveries of Magendie on venous absorption, in 1809, it was believed that all poisons produced their effects by impressions transmitted through the nerves. The chief argument in support of this view, was that the rapidity of action of certain poisons was incompatible with any other mode of transmission. Dr. Blake successfully met this argument, and showed from experiments that sufficient time elapsed for absorption even

in the case of those substances the most rapid in their action, such as hydrocyanic acid and conine. Through the labors and experiments of Dr. Blake, Sir Benj. Brodie, Sir Robert Christison, M. Bernard, and other physiologists, the views of Magendie were confirmed, and it was accepted that the entrance of the poison into the blood was a condition essential to its action.

That certain substances were absorbed and widely distributed, was early observed from the color imparted to various tissues of the body, and to the urine, by certain coloring principles, as indigo, picric acid, and the like; and by the characteristic odor perceived throughout the body in poisoning by prussic acid and other odorous substances. When we consider how minute is the quantity of certain poisons required to destroy life, the imperfect character of the methods of analysis early employed, and the fact that certain poisons may soon pass beyond recovery, it is not surprising that the progress in recovering poisons from the blood and tissues was somewhat slow. We find, however, that in 1821, Tiedeman and Gmelin found lead, mercury, and barium in the blood of animals poisoned by salts of these metals; that, in 1827, Wöhler recovered certain administered poisons from the urine; and that, in 1829, Wibmer satisfactorily proved the presence of lead in the tissues of animals poisoned by that metal. It was reserved, however, for Professor Orfila, whose original and profound labors in this department have brought honor upon science, to show the absorption and distribution of arsenic throughout the animal body. In January, 1839, this distinguished investigator announced to the Parisian Academy of Medicine, that in poisoning by this substance, the arsenic diffuses itself in such quantity that it may be recovered by chemical methods from the blood, tissues, and various secretions of the body. In 1840, he proved these facts to the satisfaction of a committee of the Academy. This discovery inaugurated a new era in medical jurisprudence. Subsequently, Orfila proved that the same wide distribution of poison throughout the body held in regard to mercury, antimony, lead, and other metallic poisons.

It has generally been believed that in the absorption of metallic poisons, and in their deposition in the soft tissues of the body, a larger proportion is to be found in the liver than in any other part, the least proportion being found in the muscles; but, according to the quite recent researches of M. Scelosubroff, absorbed arsenic, both in acute and chronic poisoning, is deposited specially in the nervous system. Thus, if the quantity found in the fresh muscle be taken as 1, that in the liver is 10.8; that in the brain 36.5; and that in the spinal marrow 37.3 (*Ann. d'Hygiène*, Jan. 1876). Under the present improved methods of analysis, it now rarely happens, in cases of poisoning by mineral substances, that the poison cannot readily be detected in the various organs and tissues of the body; yet it is well known that even in this kind of poisoning the toxic agent may be entirely removed from the body prior to death.

Our experience in regard to the recovery of the vegetable poisons has not been so satisfactory. While there are some of this class which may be readily detected in the blood and tissues, and others that have been found only rarely, there is still a large number that have never as yet been found in the absorbed state.

That all the organic poisons enter the blood and are diffused throughout the body is no longer doubted. The first instance of the recovery of a vegetable alkaloid, after it had undergone absorption, was announced by Stas, as late as in 1845, and less than a third of a century ago; in this



case he recovered morphine from the viscera of a body that had been buried for thirteen months. Many instances have occurred since, however, in which, even under more favorable conditions, there has been a total failure to recover this alkaloid from any part of the body. So, also, in 1851, Stas detected nicotine in the blood of a dog poisoned by that substance, employing his ether process for the extraction of the alkaloid.

Perhaps no one circumstance did so much to call the attention of toxicologists to the subject of the detection of the vegetable poisons in the blood and tissues, as the remarkable trial, in London, of Palmer for the poisoning of Cook by strychnine, in 1856. Prior to May, 1856, according to Prof. A. S. Taylor, in no instance had strychnine been recovered in an absorbed state from the blood, tissues, or soft organs of the body. This trial directed special attention to this poison, and led to its more careful investigation, and from that time instances of its recovery after absorption have become quite frequent. In fact, under the recent improved methods of analysis, a failure to recover this poison in its absorbed state, should rarely happen. Since this time, chemists have been gradually adding to their triumphs in this important department of research, and now authentic instances have been recorded of the recovery and identification by chemical tests, of at least the following alkaloids: morphine, nicotine, strychnine, brucine, atropine, daturine, veratrine, jervine, and conine. It may be added, that considerable difference exists in regard to the readiness with which the different poisons just mentioned may be recovered when in the absorbed state.

That all poisons, except those endowed with corrosive action, have to enter the circulation in certain quantity before producing their peculiar effects, is now universally conceded. We may now inquire what is known of the mode or manner in which when diffused in the blood they destroy life. It is well known that some poisons produce an appreciable change in the physical and chemical properties of the blood, as shown in the difference of color and consistency of that fluid. These changes are well marked in the cases of sulphuretted hydrogen, prussic acid, carbonic acid, chloroform, and conine, under the action of which the blood becomes more liquid and of a darker color. In most of these cases the poisoned blood, when examined by the spectroscope, gives the spectrum of deoxidized blood.

It was long since observed that certain poisons on being introduced into the blood were either wholly, or in great part, decomposed. Thus, Sir R. Christison failed to obtain any chemical evidence of the presence of oxalic acid in the blood of the vena cava of a dog, killed in thirty seconds by the injection of eight grains and a half of that poison into the femoral vein. Even with the improved methods of analysis, chemists have never yet been able to recover this poison, as such, from the blood. In some cases we can very clearly trace the changes which take place in the substance absorbed by the blood. Thus Erdmann and Marchand, in 1842, found that cinnamic acid was converted during its progress through the animal system into hippuric acid; and in 1862, Dr. Letheby found that under like conditions nitro-benzole was changed into aniline. In like manner it has been found that hydride of benzole is changed into benzoic acid, which in its turn becomes converted into hippuric acid. In 1832, Liebig showed that hydrate of chloral under the action of an alkali, was changed into chloroform and formic acid; and in 1868, Liebrich showed that the same change took place when this substance

entered the blood by absorption, and to this change is attributed the peculiar sedative effects of chloral.

Even in regard to the action of strychnine, brucine, morphine, veratrine, nicotine, and certain other organic poisons, which may be recovered from the blood in their unchanged state, it has been claimed by some that they are changed in part at least before they produce their toxic effect, but of this there is no direct proof. When we consider the extremely minute quantity of substances of this kind which may destroy life (a quantity sometimes certainly not exceeding in weight the one three hundred thousandth part of the blood), and the ready demonstration of their presence in the blood after death, it would appear that in certain instances at least, the fatal issue is not dependent upon the decomposition of any part of the toxic agent.

Although the various facts that have been presented are of great value and interest, yet it must be admitted that the whole subject of the final action of poisons is left in great obscurity. While it is believed by all that poisons are absorbed and taken into the circulation, it is found that only some produce any marked changes, physical or chemical, in the blood; and on the other hand, while some poisons are themselves decomposed in that liquid, yet others equally fatal, appear to suffer little or no change. We may trace the destroyer in all its subtle insinuations through the blood and tissues, and see life quickly driven from the body, but we know not *where* nor *how* the fatal stroke is given. These are questions which modern science, with all its refined methods of research, has left unanswered.

In conclusion, it may be said that the field in which the toxicological chemist labors, is one of the highest responsibility. He must not only be consecrated to his science, know all its best methods, and be able to practise them in all their most delicate and skilful manipulations; but he should have a higher consecration to *truth*, ever remembering that in toxicological jurisprudence his words should be weighed in balances even more delicate and exact than those in which he weighs his material substances. Human life on the one hand, and the security of society and the vindication of law on the other, may hang upon the slender thread of a chemical reaction, or tremble in the final adjustment of a most delicate instrument. The highest skill, and a regard for truth that knows no shadow of turning, can alone fit the toxicological chemist to meet the grave responsibilities of his profession.











